580.439 Midterm solutions, 1999

Problem 1:

Part 1: If the ions are at equilibrium, then the boundary potentials must be given in terms of the concentrations by the Nernst equation:

$$V_B = E_K = \frac{RT}{F}\ln\frac{C_{soln}}{K_{membr}} = E_{Cl} = -\frac{RT}{F}\ln\frac{C_{soln}}{Cl_{membr}} \qquad (1)$$

This expression is the same at both boundaries of the membrane. C_{soln} has been substituted for both the potassium and chloride concentrations in solution. K_{membr} and Cl_{membr} are the (unknown) potassium and chloride concentrations in the membrane. Note that both potassium and chloride must have the same equilibrium potential across the boundary.

Part 2: Charge electroneutrality holds automatically in solution, where both the potassium and chloride concentrations are given by C_{soln}. In the membrane,

$$K_{membr} = N + Cl_{membr} \qquad (2)$$

Equations 1 and 2 now have three unknowns, V_B, K_{membr}, and Cl_{membr}. To solve these equations, note that Eqn. 1 implies that:

$$K_{membr}Cl_{membr} = C_{soln}^2 \qquad (3)$$

Eliminating Cl_{membr} in Eqn. 2 using Eqn. 3 gives

$$K_{membr} = N + \frac{C_{soln}^2}{K_{membr}}$$

$$K_{membr}^2 - NK_{membr} - C_{soln}^2 = 0$$

$$K_{membr} = \frac{N}{2} \pm \sqrt{\frac{N^2}{4} + C_{soln}^2} \qquad (4)$$

Equation 4 is the solution for K_{membr} from the quadratic theorem. Of the two solutions, the one with the negative sign gives a net negative potassium concentration in the membrane, so only the solution with the positive sign is physically valid. Given Eqn. 4, the remaining variables can be determined using Eqns. 1 and 2:

$$K_{membr} = \frac{N}{2} + \sqrt{\frac{N^2}{4} + C_{soln}^2} \qquad Cl_{membr} = \sqrt{\frac{N^2}{4} + C_{soln}^2} - \frac{N}{2} \qquad V_B = \frac{RT}{F}\ln\frac{C_{soln}}{\frac{N}{2} + \sqrt{\frac{N^2}{4} + C_{soln}^2}} \qquad (5)$$

Part 3: In class, the following equation was derived by integrating the Nernst-Planck equation across a diffusion regime like the interior of the membrane in this problem:

$$I_i \int_0^d \frac{dx}{z_i^2 F^2 u_i C_i} = V - E_i$$

where I_i is the current density for ion i through the regime, C_i is its concentration, and V is the electrical potential across the regime. E_i is the equilibrium potential for the ion, which is 0 in this case. The integral is the resistance to flow of current carried by ion i. Usually, the integral cannot be evaluated because C_i is an unknown function of x, the distance through the membrane. In this case, however C_i is known and constant, as given by Eqn. 5, so

$$\begin{aligned} R_K &= \int_0^d \frac{dx}{F^2 u_K K_{membr}} = \frac{d}{F^2 u_K \left[N/2 + \sqrt{N^2/4 + C_{soln}^2} \right]} \\ R_{Cl} &= \int_0^d \frac{dx}{F^2 u_{Cl} Cl_{membr}} = \frac{d}{F^2 u_{Cl} \left[\sqrt{N^2/4 + C_{soln}^2} - N/2 \right]} \end{aligned} \tag{6}$$

It is possible to derive these expressions directly from the Nernst-Planck equation by noting that the concentrations in the membrane are constant, so $d\ln C/dx=0$ and

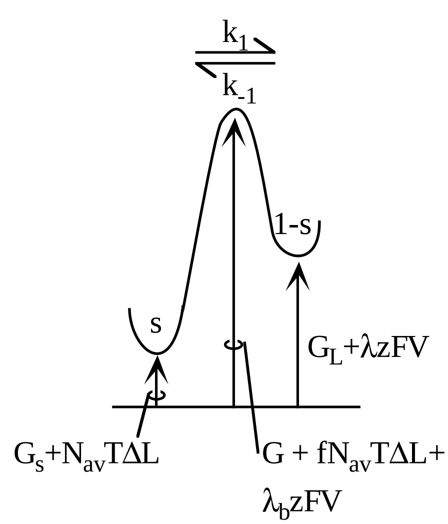
$$I_i = z_i F u_i C_i \left[RT \frac{d \ln C_i}{dx} + z_i F \frac{dV}{dx} \right] = u_i C_i z_i^2 F^2 \frac{dV}{dx}$$

which can be integrated across the membrane as follows (assuming the steady state as usual, so that I_i is constant):

$$\int_0^d \frac{I_i\, dx}{u_i C_i z_i^2 F^2} = \frac{I_i}{u_i C_i z_i^2 F^2} \int_0^d dx = \int_0^V dV$$

from which Eqns 6 follow directly.

Problem 2:



Part 1: It takes work to contract the channel to the short configuration, so the energy of the membrane system is increased by that amount of work (equal to $T\Delta L$, the force times the distance of the contraction of the protein, for each molecule, or $N_{av}T\Delta L$ per mole, where N_{av} is Avagadro's number) when it is in the short mode, relative to the long mode. The membrane potential increases the energy of the long mode by λzFV where λ is the fraction of the membrane potential through which the plug moves in going from short to the long mode and z is the charge on the plug. At the barrier, a

fraction f of the mechanical energy and λ_b of the electrical energy has been added to the system. The barrier diagram with mechanical and electrical effects added is shown at right above. Note that the zero position on the energy axis is arbitrary, since only energy differences between peaks and valleys count. Thus it is not necessary to compute the total potential energy due to the tension in the membrane, only the change in energy when the plug moves. Similarly, it is only the change in electrical potential energy seen when the plug moves that counts.

Part 2: Using the rate constants defined above,

$$\frac{ds}{dt} = k_{-1}(1-s) - k_1 s = k_{-1} - (k_1 + k_{-1})s$$

$$= \alpha e^{-(G-G_L + fN_{av}T\Delta L + \lambda_b zFV - \lambda zFV)/RT} - \left(\alpha e^{-(G-G_S + fN_{av}T\Delta L - N_{av}T\Delta L + \lambda_b zFV)/RT} + \alpha e^{-(G-G_L + fN_{av}T\Delta L + \lambda_b zFV - \lambda zFV)/RT}\right)s \tag{7}$$

Part 3: When ds/dt=0, the steady-state value of s, denoted $s(t \to \infty)$ is

$$0 = \alpha e^{-(G-G_L + fN_{av}T\Delta L + \lambda_b zFV - \lambda zFV)/RT} - \left(\alpha e^{-(G-G_S + fN_{av}T\Delta L - N_{av}T\Delta L + \lambda_b zFV)/RT} + \alpha e^{-(G-G_L + fN_{av}T\Delta L + \lambda_b zFV - \lambda zFV)/RT}\right)s(t \to \infty)$$

$$s(t \to \infty) = \frac{\alpha e^{-(G-G_L + fN_{av}T\Delta L + \lambda_b zFV - \lambda zFV)/RT}}{\alpha e^{-(G-G_S + fN_{av}T\Delta L - N_{av}T\Delta L + \lambda_b zFV)/RT} + \alpha e^{-(G-G_L + fN_{av}T\Delta L + \lambda_b zFV - \lambda zFV)/RT}}$$

$$= \frac{1}{1 + e^{(G_S - G_L + N_{av}T\Delta L - \lambda zFV)/RT}} \tag{8}$$

The function in Eqn. 8 is the same as the m_∞, n_∞, and h_∞ functions of the Hodgkin-Huxley equations. Denoting Eqn. 8 as s_∞ and using the expression for time constant in Eqn. 10 below, the differential equation for s can bewritten in a familiar form as

$$\frac{ds}{dt} = \frac{s_\infty(V,T) - s}{\tau_s(V,T)} \tag{9}$$

Part 4: When a step in either V or T is applied, the steady state value of s changes, according to Eqn. 8 and s undergoes an exponential decay to its new steady state value. That is, the solution to the first-order differential equation in Eqn. 7 or 9 is an exponential decay. The time constant of the decay is $1/(k_1+k_{-1})$ which is

$$\tau_s(V,T) = \frac{1}{\alpha e^{-(G-G_S + fN_{av}T\Delta L - N_{av}T\Delta L + \lambda_b zFV)/RT} + \alpha e^{-(G-G_L + fN_{av}T\Delta L + \lambda_b zFV - \lambda zFV)/RT}}$$

$$= \frac{1}{\alpha\, e^{-(G + fN_{av}T\Delta L + \lambda_b zFV)/RT}\left[e^{(G_S + N_{av}T\Delta L)/RT} + e^{(G_L + \lambda zFV)/RT}\right]} \tag{10}$$

The current which is observed is the charge on the plug moving in the membrane. When the membane is depolarized (*V* increased), the *s* state is favored and the plugs move outward, giving a positive current, as seen in A of the problem statement. When *T* is increased, state *s* is disfavored and there is a net inward movement of plugs, giving a negative current. This is exactly the same as a gating current.

Part 5: If there is no change in Eqn. 8, i.e. in $s_\infty(V,T)$, then there will be no change in *s*. From Eqn. 8, $s_\infty(V,T)$ is constant if the exponent of the exponential in the denominator is constant, which requires that:

$$\Delta\left(N_{av}T\,\Delta L-\lambda zF\,V\right)=N_{av}\Delta T\,\Delta L-\lambda zF\,\Delta V=0 \quad \text{or} \quad \frac{\Delta \mathrm{T}}{\Delta \mathrm{V}}=\frac{\lambda zF}{N_{av}\Delta L}$$